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Monsanto

ENVIRONMENT, SAFETY & HEALTH

Monsanto Company
800 N. Lindbergh Boulevard
St. Louis, Missouri 63167
Phone: (314) 694-1000

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8EHQ-92-12292

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April 6, 1993

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Office of Toxic Substances
Environmental Protection Agency
401 M Street, NW
Washington, DC 20460

Attn: Section 8(e) Coordinator (CAP Agreement)

On June 10, 1992 Monsanto submitted copies of study No. Y-69-5 for the chemical designated below. I was recently informed by a Ms. Jennifer Welham at EPA that the copies of the study were incomplete. Enclosed are complete copies of the study.

This submission is pursuant to the TSCA Section 8(e) Compliance Audit Program and CAP Agreement #8ECAP-0036.

The information included herein is characterized as follows:

Chemical Identity: 2,6-diethyl phenylazomethine

Chemical CAS No.: 35203-08-8

Information/Study Type: II,B,2,b

Information/Study Identification: Dermal LD_{50}, Y-69-5

Summary of reportable adverse effects: Submitted due to a moderate order of dermal toxicity in a test material that has a potential for considerable human exposure.

Previous TSCA 8(e) or PMN submissions for the reference chemical: See 8(e) docket 8EHQ-0490-0927S; TR-84-039 Pilot Rat Teratology; ML-86-360 Rat Reproduction.

It should be noted that this summary may not highlight all adverse effects that EPA may judge to meet TSCA 8(e) reportability.

No information contained in this submission is trade secret or confidential business information.

Sincerely,

J. R. Condray
Director, Regulatory Management
(314) 694-8883

cap-cor.046

RECEIVED 2/24/95

PROJECT NO.
REPORT FILE

YOUNGER LABORATORIES

Biochemists . . . Pharmacologists . . . Analysts

125 CLIFF CAVE ROAD
SAINT LOUIS, MO., 63129
PHONE: TILDEN 6-2540

Certificate of Analysis

February 6th, 1969

SUBJECT - [redacted]

Toxicological Investigation Of: 2,6-Diethylaniline Ammonium

Monsanto Sample Number 6

Monsanto Project Number Y-69-5

STUDY CONDUCTED FOR -

Monsanto Company, St. Louis, Missouri

EXPERIMENTAL PROCEDURE -

A) Oral LD_{50} (Rats, Mixed Sex)

The undiluted compound was fed by stomach tube to Sprague-Dawley strain albino male and female rats.

After the approximate Minimum Lethal Dose was determined, groups of male and female rats were fed in increasing doses at increments of 0.1 fractional log intervals at four levels designed to bracket the toxicity range thereby supplying data for calculation of the LD_{50} which was done according to a modification of the method of E. J. de Beer.

Observations were made for toxic symptoms and the viscera of the test animals were examined macroscopically.

The data are shown in Table I.

B) Skin Absorption MLD (Rabbits, Mixed Sex)

The undiluted compound was applied in increasing doses at increments of 0.2 fractional log intervals to the closely clipped, intact skin of New Zealand white male and female rabbits.

The treated areas were covered with plastic strips and the animals held in wooden stocks for periods up to twenty-four hours, after which time they were assigned to individual cages.

Observations were made for toxic symptoms and the viscera of the test animals were examined macroscopically.

The data are shown in Table II.

EXPERIMENTAL PROCEDURE - (Continued)

C) Skin Irritation (Rabbits, Mixed Sex)

The undiluted compound was applied to the clipped, intact skin of albino male and female rabbits and removed after twenty-four hours. The application was covered with plastic strips to retard evaporation and avoid contamination.

Observations were made over a period of several days for irritation.

The data, scored according to the method of Draize, Woodard and Calvery (Journal of Pharm. and Exp. Therapeutics, Volume 82, December, 1944) are shown in Table III.

D) Eye Irritation (Rabbits, Mixed Sex)

0.1 Milliliter of undiluted sample was placed in the conjunctival sac of the right eye of each of three albino male and female rabbits and observations made over a period of several days for inflammation.

The eyes were rinsed with warm isotonic saline solution after twenty-four hours.

The data, scored according to the method of Draize, et al, are shown in Table IV.

E) Vapor Inhalation (Male Rats)

Four 150-gram male rats were placed in a glass desiccator, 250 cm in diameter, and exposed for six hours to a concentrated atmosphere of vapors produced by passing a stream of air through 67.4 grams of the compound contained in a 250-milliliter erlenmeyer flask. Vapors from the flask passed into a one liter bottle to remove droplets and then into the chamber.

Air flow through the sample was four liters per minute as measured by a calibrated rotameter. This was sufficient to violently agitate the liquid. No supplementary air was introduced inasmuch as the above supply was ample for the animals oxygen requirements.

The animals were observed for behavior and since there were no deaths, all were held for ten days observation then sacrificed. The viscera were examined macroscopically.

The data are shown in Table V.

SUMMARY -

2,6-Diethylaniline Azomethine

A) Oral LD_{50} (Rats, Mixed Sex)

The Oral LD_{50} for male and female rats was placed at 1490 milligrams per kilogram with lower and upper limits of 1340 to 1660 milligrams per kilogram.

The compound was classed as mildly toxic by oral ingestion in male and female rats.

SUMMARY - (Continued)

B) Skin Absorption MLD (Rabbits, Mixed Sex)

The Minimum Lethal Dose by Skin Absorption in male and female rabbits was found to be greater than 501 milligrams per kilogram and less than 794 milligrams per kilogram.

The compound was classed as moderately toxic by skin absorption in male and female rabbits.

C) Skin Irritation (Rabbits, Mixed Sex)

The compound was classed as a moderate irritant when applied undiluted to intact skin of male and female rabbits.

The average maximum score was 3.6 out of a possible 8 in twenty-four hours.

D) Eye Irritation (Rabbits, Mixed Sex)

The compound was classed as a severe eye irritant in male and female rabbits.

The average maximum score was 61.6 out of a possible 110 in twenty-four hours.

E) Vapor Inhalation (Male Rats)

All animals survived the six hour exposure as well as the following ten day observation period.

It was concluded that the vapors were mildly toxic under conditions of the test.

YOUNGER LABORATORIES

BY: MELVIN D. BIRCH

To: Monsanto Company
St. Louis, Missouri
Younger Laboratories Certificate of Analysis - Page 4 (2/6/69) - L-69-5

TABLE I

THE ORAL LD_{50} OF

'2,6-Diethylaniline Acetethine' FOR RATS

Sample Fed Undiluted

Animal No. - Sex	Weight Gm.	Dose Mg./Kg.	Fate
1- Female	235	1000	Survived
2- Male	250	1000	Died
3- Female	210	1000	Survived
4- Male	230	1000	Survived
5- Female	205	1000	Survived
6- Male	245	1260	Survived
7- Female	220	1260	Survived
8- Male	240	1260	Died
9- Female	190	1260	Died
10- Male	225	1260	Survived
11- Female	210	1580	Died
12- Male	220	1580	Survived
13- Female	225	1580	Died
14- Male	240	1580	Died
15- Female	215	1580	Died
16- Male	250	2000	Died
17- Female	195	2000	Died
18- Male	235	2000	Died
19- Female	220	2000	Died
20- Male	225	2000	Survived

DISCUSSION -

The Oral LD_{50} for male and female rats was placed at 1490 milligrams per kilogram with lower and upper limits of 1340 to 1660 milligrams per kilogram.

The compound was classed as mildly toxic by oral ingestion in male and female rats.

Survival time was one to four days with most deaths occurring in two to three days.

Toxic symptoms included reduced activity, poor appetite, weakness, and collapse.

At autopsy there was hemorrhagic areas in the lungs, liver, and kidneys by macroscopic examination.

Surviving animals were sacrificed nine days after dosing. Macroscopic examination revealed mottled areas of the liver and hemorrhagic areas in the lungs.

TABLE II

THE MINIMUM LETHAL DOSE OF '2,6-Diethylaniline Anesthine' BY SKIN ABSORPTION IN RABBITS

Sample Applied Undiluted

Animal No. - Sex	Weight Kg.	Dose Mg./Kg.	Weight Change 5 Days Later Kg.	Fate
1 - Male	2.3	200	+ 0.1	Survived
2 - Female	2.1	316	+ 0.1	Survived
3 - Male	2.4	501	+ 0.1	Survived
4 - Female	2.1	794	-----	Died -- 4 Days
5 - Male	2.2	1260	-----	Died -- 5 Days
6 - Female	1.9	2000	-----	Died -- 2 Days

DISCUSSION -

The Minimum Lethal Dose by Skin Absorption in male and female rabbits was found to be greater than 501 milligrams per kilogram and less than 794 milligrams per kilogram.

The compound was classed as moderately toxic by skin absorption in male and female rabbits.

Survival time was two to five days.

Toxic symptoms included weakness and collapse in twelve hours to two days in animals #4 through #6. Reduced appetite and activity were present in the survivors for two to three days.

At autopsy there was congestion of the liver and lungs macroscopically.

Surviving animals were sacrificed fourteen days after dosing. The viscera appeared normal by macroscopic examination.

TABLE III

SKIN IRRITATION IN RABBITS AFTER APPLICATION OF
'2,6-Diethylaniline Azomethine'

Sample Applied Undiluted

Animal No. - Sex	Numerical Evaluation At The End Of 1 Hour	24 Hours	48 Hours	72 Hours	120 Hours	168 Hours
1 - Male	3	4	1	0	0	0
2 - Female	2	3	0	0	0	0
3 - Male	3	4	1	0	0	0
Average	2.6	3.6	0.6	0.0	0.0	0.0

DISCUSSION -

The compound was classed as a moderate irritant when applied undiluted to intact skin of male and female rabbits.

The average maximum score was 3.6 out of a possible 8 in twenty-four hours.

Well-defined erythema with no edema was recorded in one hour.
In twenty-four hours redness remained the same but there was mild edema on all animals.
Slight redness was still present on two of three animals in forty-eight hours.
All animals received a zero within seventy-two hours.

TABLE IV

EYE IRRITATION IN RABBITS AFTER APPLICATION OF '2,6-Diethylaniline Anomethine'

Sample (0.1 Milliliter) Applied Undiluted

Animal No. - Sex	Numerical Evaluation At The End Of 1 Hour	24 Hours	48 Hours	72 Hours	120 Hours	168 Hours
1 - Male	18	65	41	30	8	4
2 - Female	16	63	45	35	10	4
3 - Male	14	57	38	26	6	2
Average	16.0	61.6	41.3	30.6	8.0	3.0

DISCUSSION -

The compound was classed as a severe eye irritant in male and female rabbits. The average maximum score was 61.6 out of a possible 110 in twenty-four hours.

Considerable discomfort including pawing, inability to open lids, and squealing by one animal was recorded immediately following application.
Within five to ten minutes there was marked erythema, slight edema, and mild lacrimation.

There was marked erythema and edema with partial eversion of the lids in one hour. Lacrimation had ceased.

In twenty-four hours there was sufficient corneal cloudiness to moderately obscure iris details, copious whitish discharge, and the iris gave a sluggish reaction to light. Erythema and edema remained the same as for the one hour reading.
After irrigation there was continued improvement so that on the fifth day iris reaction was normal and corneal clarity was restored. Slight edema and moderate erythema remained.
In seven days only slight to mild redness remained.

TABLE V

INHALATION OF 2,6-Diethylaniline Azomethine' VAPORS BY RATS

Average Temperature Inside Chamber ..... 74° F.

Average Relative Humidity Inside Chamber ..... 54 %

Amount of Sample -- To start ..... 67.4 Grams
Recovered ..... 66.2 Grams
Vaporized or left in equipment ..... 1.2 Grams (1.8%)

Animal No. - Sex	Fate	Observations During Exposure
1 - Male	Survived	There was immediate discomfort including pawing, inability to open eyes, nasal and ocular discharge ...
2 - Male	Survived	In thirty minutes there was difficult breathing, slight lethargy, reduced activity, slow reflexes ...
3 - Male	Survived	There was slight improvement toward end of test.
4 - Male	Survived	

...SION -

All animals survived the six hour exposure as well as the following ten day observation period.

It was concluded that the vapors were mildly toxic under conditions of the test.

There was considerable discomfort immediately including pawing, nasal and ocular discharge, and inability to open eyes.

In thirty minutes there was difficult breathing and slight lethargy, reduced activity, and slow reflexes.

These conditions continued throughout the inhalation time with some slight improvement toward the end.

Slight bronchial rales were present when the animals were removed from the chamber and continued for three to four days.

All animals survived the ten day observation period and were in good health at that time.

The following animals were sacrificed ten days after test. Macroscopic examination revealed areas of pulmonary congestion and slight liver discoloration.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

J. R. Condray
Director, Regulatory Management
Monsanto Company
800 North Lindbergh Boulevard
St. Louis, Missouri 63167

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

APR 18 1995

EPA acknowledges the receipt of information submitted by your organization under Section 8(e) of the Toxic Substances Control Act (TSCA). For your reference, copies of the first page(s) of your submission(s) are enclosed and display the TSCA §8(e) Document Control Number (e.g., 8EHQ-00-0000) assigned by EPA to your submission(s). Please cite the assigned 8(e) number when submitting follow-up or supplemental information and refer to the reverse side of this page for "EPA Information Requests".

All TSCA 8(e) submissions are placed in the public files unless confidentiality is claimed according to the procedures outlined in Part X of EPA's TSCA §8(e) policy statement (43 FR 11110, March 16, 1978). Confidential submissions received pursuant to the TSCA §8(e) Compliance Audit Program (CAP) should already contain information supporting confidentiality claims. This information is required and should be submitted if not done so previously. To substantiate claims, submit responses to the questions in the enclosure "Support Information for Confidentiality Claims". This same enclosure is used to support confidentiality claims for non-CAP submissions.

Please address any further correspondence with the Agency related to this TSCA 8(e) submission to:

Document Processing Center (7407)
Attn: TSCA Section 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
Washington, D.C. 20460-0001

EPA looks forward to continued cooperation with your organization in its ongoing efforts to evaluate and manage potential risks posed by chemicals to health and the environment.

Sincerely,

Terry R. O'Bryan

Terry R. O'Bryan
Risk Analysis Branch

Enclosure 12292A

Triage of 8(e) Submissions

Date sent to triage: APR 20 1995 NON-CAP (CAP)

Submission number: 12292 A TSCA Inventory: (Y) N D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO AQUATO

Group 2 - Ernie Falke (1 copy total)

(ATOX) SBTOX SEN w/NEUR

Group 3 - Elizabeth Margosches (1 copy each)

STOX CTOX EPI RTOX GTOX

STOX/ONCO CTOX/ONCO IMMUNO CYTO NEUR

Other (FATE, EXPO, MET, etc.): _____

Notes:

THIS IS THE ORIGINAL 8(e) SUBMISSION; PLEASE REFILE AFTER TRIAGE DATABASE ENTRY

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entire document: (0) 1 2 **pages** 1 **pages** 1, THKS

Notes:

Contractor reviewer : PJK **Date:** 4/3/95

CECATS\TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA:
Submission # 8EHQ- 0493 - 12292 SEQ. A

TYPE: (INT.) SUPP FLWP

SUBMITTER NAME: Monsanto Company

INFORMATION REQUESTED: FLWP DATE:
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL. ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:
(0639) REFER TO CHEMICAL SCREENING
0678 CAP NOTICE

VOLUNTARY ACTIONS:
(0401) NO ACTION REPORTED
0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKERS/USERS
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP./USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

SUB. DATE: 04/06/93 OTS DATE: 04/15/93 CSRAD DATE: 02/24/95

CHEMICAL NAME:

CAS#
35203-08-8

INFORMATION TYPE:		P F C
0201	ONCO (HUMAN)	01 02 04
0202	ONCO (ANIMAL)	01 02 04
0203	CELL TRANS (IN VITRO)	01 02 04
0204	MUTA (IN VITRO)	01 02 04
0205	MUTA (IN VIVO)	01 02 04
0206	REPRO/TERATO (HUMAN)	01 02 04
0207	REPRO/TERATO (ANIMAL)	01 02 04
0208	NEURO (HUMAN)	01 02 04
0209	NEURO (ANIMAL)	01 02 04
0210	ACUTE TOX. (HUMAN)	01 02 04
0211	CHR. TOX. (HUMAN)	01 02 04
(0212)	ACUTE TOX. (ANIMAL)	01 02 04
0213	SUB ACUTE TOX (ANIMAL)	01 02 04
0214	SUB CHRONIC TOX (ANIMAL)	01 02 04
0215	CHRONIC TOX (ANIMAL)	01 02 04

INFORMATION TYPE:		P F C
0216	EPI/CLIN	01 02 04
0217	HUMAN EXPOS (PROD CONTAM)	01 02 04
0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04
0219	HUMAN EXPOS (MONITORING)	01 02 04
0220	ECO/AQUA TOX	01 02 04
0221	ENV. OCCC/REL/FATE	01 02 04
0222	EMER INCI OF ENV CONTAM	01 02 04
0223	RESPONSE REQEST DELAY	01 02 04
0224	PROD/COMP/CHEM ID	01 02 04
0225	REPORTING RATIONALE	01 02 04
0226	CONFIDENTIAL	01 02 04
0227	ALLERG (HUMAN)	01 02 04
0228	ALLERG (ANIMAL)	01 02 04
0239	METAB/PHARMACO (ANIMAL)	01 02 04
0240	METAB/PHARMACO (HUMAN)	01 02 04

INFORMATION TYPE:		P F C
0241	IMMUNO (ANIMAL)	01 02 04
0242	IMMUNO (HUMAN)	01 02 04
0243	CHEM/PHYS PROP	01 02 04
0244	CLASTO (IN VITRO)	01 02 04
0245	CLASTO (ANIMAL)	01 02 04
0246	CLASTO (HUMAN)	01 02 04
0247	DNA DAM/REPAIR	01 02 04
0248	PROD/USE/PROC	01 02 04
0251	MSDS	01 02 04
0299	OTHER	01 02 04

TRIAGE DATA: NON-CBI INVENTORY
(YES)
CAS SR NO
IN TRANSIT

ONGOING REVIEW
YES (DROP/REFER)
NO (CONTINUE)
REFER

SPECIES
RAT
RBT

TOXICOLOGICAL CONCERN:
LOW
(MED)
HIGH

USE:

PRODUCTION:

COMMENTS: Beha - 0490-09275

8(E)-12292A

L/L/M/M/M

ACUTE ORAL TOXICITY IN SPRAGUE-DAWLEY RATS IS OF LOW CONCERN BASED ON AN LD50 OF 1490 MG/KG. DOSAGE (GAVAGE) AND MORTALITY DATA ARE AS FOLLOWS: 1000 MG/KG (1/2 M, 0/3 F); 1260 MG/KG (1/3 M, 1/2 F); 1580 MG/KG (1/2 M, 3/3 F); AND 2000 MG/KG (2/3 M, 2/2 F). CLINICAL SIGNS INCLUDED REDUCED ACTIVITY, POOR APPETITE, WEAKNESS, AND COLLAPSE. GROSS PATHOLOGICAL SIGNS INCLUDED HEMORRHAGIC AREAS IN THE LUNGS, LIVER, AND KIDNEYS.

ACUTE INHALATION TOXICITY IN RATS IS OF LOW CONCERN. DOSAGE (6-HOURS) WAS NOT REPORTED; MORTALITY WAS 0/4 MALE. IMMEDIATE CLINICAL SIGNS WERE DISCOMFORT INCLUDING PAWING, INABILITY TO OPEN EYES, AND NASAL AND OCULAR DISCHARGE. AFTER 30-MINUTES, CLINICAL SIGNS INCLUDED DIFFICULTY IN BREATHING, SLIGHT LETHARGY, REDUCED ACTIVITY, AND SLOW REFLEXES. THERE WAS SLIGHT IMPROVEMENT TOWARD END OF TEST. GROSS PATHOLOGICAL SIGNS INCLUDED PULMONARY CONGESTION AND LIVER DISCOLORATION.

ACUTE DERMAL TOXICITY IN RABBITS IS OF MEDIUM CONCERN BASED ON AN LD50 BETWEEN 501 MG/KG AND 794 MG/KG. DOSAGE AND MORTALITY DATA ARE AS FOLLOWS: 200 MG/KG (0/1 M); 316 MG/KG (0/1 F); 501 MG/KG (0/1 M); 794 MG/KG (1/1 F); 1260 MG/KG (1/1 M); AND 2000 MG/KG (1/1 F). CLINICAL SIGNS INCLUDED WEAKNESS, COLLAPSE, REDUCED APPETITE AND ACTIVITY. GROSS PATHOLOGICAL SIGNS INCLUDED CONGESTION IN THE LUNGS AND LIVER.

ACUTE DERMAL IRRITATION IN RABBITS IS OF MEDIUM CONCERN BASED ON MODERATE IRRITATION AND A WELL-DEFINED ERYTHEMA WITH NO EDEMA (2/2 M, 1/1 F) FROM A 24-HOUR OCCLUDED EXPOSURE TO A SINGLE DOSE (AMOUNT NOT REPORTED).

ACUTE EYE IRRITATION IN RABBITS IS OF MEDIUM CONCERN BASED ON SEVERE IRRITATION (DRAIZE SCORE OF 61.6/110 AT 24 HOURS). ERYTHEMA, SLIGHT EDEMA, AND MILD LACRIMATION (2/2 M, 1/1 F) OCCURRED FROM A 24-HOUR EXPOSURE TO 0.1 ML. AFTER 24-HOURS, THERE WAS CORNEAL CLOUDINESS AND COPIOUS WHITISH DISCHARGE, BUT IRIS REACTION WAS NORMAL AND CORNEAL CLARITY WAS RESTORED BY THE FIFTH DAY.